

WE CLAIM:

1. A method of producing transduced mammalian T cells or non-dividing cells, the
5 method comprising:
 - (a) obtaining a population of T cells or non-dividing cells from a patient; and
 - (b) transducing the population of T cells or non-dividing cells *ex vivo* with a
preparation of high titer recombinant retroviral particles substantially free from
contamination with replication competent retrovirus, wherein the recombinant retroviral
10 particles carry a vector construct encoding a gene of interest.
2. The method of Claim 1 wherein said T cells are isolated CD4+ T cells.
3. The method of Claim 1 wherein said T cells are isolated CD8+ T cells.
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4. The method of Claim 1 wherein the gene of interest encodes a protein or active
portion of a protein selected from the group consisting of a cytokine, a colony stimulating
factor, a clotting factor, and a hormone.
- 20 5. The method of Claim 4 wherein said clotting factor is factor VIII.
6. The method of Claim 1 wherein the patient is a human suffering from a disease
selected from the group consisting of a genetic disease, a cancer, an infectious disease, an
autoimmune disease, a cardiovascular disease, degenerative disease, and an
25 inflammatory disease.
7. A composition comprising an isolated population of mammalian T cells or non-
dividing cells, transduced *ex vivo* with a preparation of high titer recombinant retroviral
particles substantially free from contamination with replication competent retrovirus,
30 wherein the recombinant particles carry a vector construct encoding a gene of interest.
8. The composition of Claim 7 wherein said T cells are isolated CD4+ T cells.
9. The composition of Claim 7 wherein said T cells are isolated CD8+ T cells.
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10. The composition of Claim 7 wherein the gene of interest encodes a protein or active portion of a protein selected from the group consisting of a cytokine, a colony stimulating factor, a clotting factor, and a hormone.

5 11. The composition of Claim 10 wherein said clotting factor is factor VIII.

12. The composition of Claim 7 wherein said mammalian cells are human cells.

10 13. A mammalian T cell or non-dividing cell transduced *ex vivo* with a preparation of high titer recombinant retroviral particles substantially free from contamination with replication competent retrovirus, wherein the recombinant retroviral particles carry a vector construct encoding a gene of interest.

15 14. The T cell of Claim 13 wherein said T cell is from an isolated population of CD4+ T cells.

15 15. The T cell of claim 13 wherein said T cell is from an isolated population of CD8+ T cells.

20 16. The T cell or non-dividing cell of Claim 13 wherein the gene of interest encodes a protein or active portion of a protein selected from the group consisting of a cytokine, a colony stimulating factor, a clotting factor, and a hormone.

25 17. The T cell or non-dividing cell of Claim 16 wherein the clotting factor is factor VIII.

18. A method of treating a patient having a genetic disease, the method comprising:

(a) obtaining a population of T cells or non-dividing cells from the patient;

30 (b) transducing the population of T cells or non-dividing cells *ex vivo* with a preparation of high titer recombinant retroviral particles substantially free from contamination with replication competent retrovirus, wherein the recombinant retroviral particles carry a vector construct encoding a gene of interest useful in treating the genetic disease; and

35 (c) re-introducing into the patient a therapeutically effective amount of the population of transduced T cells or non-dividing cells.

19. The method of claim 18 wherein said cell population is a T cell population, wherein said disease is ADA deficiency, and wherein said gene of interest is ADA.

20. The method of Claim 18 further comprising expanding the transduced population of T cells, non-dividing cells prior to re-introduction of the cells into the patient.

21. A method of treating a patient having cancer, the method comprising:

- (a) obtaining a population of T cells or non-dividing cells from the patient;
- (b) transducing the population of T cells or non-dividing cells *ex vivo* with a preparation of high titer recombinant retroviral particles substantially free from contamination with replication competent retrovirus, wherein the recombinant retroviral particles carry a vector construct encoding a gene of interest useful in treating cancer; and
- (c) re-introducing into the patient a therapeutically effective amount of the population of transduced T cells or non-dividing cells.

22. A method of treating a patient having an infectious disease, the method comprising:

- (a) obtaining a population of T cells or non-dividing cells from the patient;
- (b) transducing the population of T cells or non-dividing cells *ex vivo* with a preparation of high titer recombinant retroviral particles substantially free from contamination with replication competent retrovirus, wherein the recombinant retroviral particles carry a vector construct encoding a gene of interest useful in treating the infectious disease; and
- (c) re-introducing into the patient a therapeutically effective amount of the population of transduced T cells or non-dividing cells.

23. The method of claim 22 wherein said cell population is a T cell population, wherein said infectious disease is AIDS, and wherein said gene of interest encodes a mutant HIV protein.

24. The method of claim 22 wherein said cell population is a T cell population, wherein said infectious disease is AIDS, and wherein said gene of interest encodes a ribozyme.

25. The method of claim 22 wherein said cell population is a T cell population, wherein said infectious disease is AIDS, and wherein said gene of interest encodes a synthetic or naturally occurring T cell receptor.

5 26. A method of treating a patient having an inflammatory disease, the method comprising:

(a) obtaining a population of T cells or non-dividing cells from the patient;

(b) transducing the population of T cells or non-dividing cells *ex vivo* with a preparation of high titer recombinant retroviral particles substantially free from contamination with replication competent retrovirus, wherein the recombinant retroviral particles carry a vector construct encoding a gene of interest useful in treating the inflammatory disease; and

(c) re-introducing into the patient a therapeutically effective amount of the population of transduced T cells or non-dividing cells.

15 27. A method of treating a patient having a degenerative disease, the method comprising:

(a) obtaining a population of T cells or non-dividing cells from the patient;

(b) transducing the population of T cells or non-dividing cells *ex vivo* with a preparation of high titer recombinant retroviral particles substantially free from contamination with replication competent retrovirus, wherein the recombinant retroviral particles carry a vector construct encoding a gene of interest useful in treating the inflammatory disease; and

(c) re-introducing into the patient a therapeutically effective amount of the population of transduced T cells or non-dividing cells.

25 28. A method of treating a patient having a cardiovascular disease, the method comprising:

(a) obtaining a population of T cells or non-dividing cells from the patient;

(b) transducing the population of T cells or non-dividing cells *ex vivo* with a preparation of high titer recombinant retroviral particles substantially free from contamination with replication competent retrovirus, wherein the recombinant retroviral particles carry a vector construct encoding a gene of interest useful in treating the cardiovascular disease; and

(c) re-introducing into the patient a therapeutically effective amount of the population of transduced T cells or non-dividing cells.

29. The method of claim 26 wherein said cell population is a T cell population, wherein said cardiovascular disease is hyperlipidemia, and wherein said gene of interest encodes apolipoprotein E.

30. A method of treating a patient having an autoimmune disease, the method comprising:

- (a) obtaining a population of T cells or non-dividing cells from the patient;
- (b) transducing the population of T cells or non-dividing cells *ex vivo* with a preparation of high titer recombinant retroviral particles substantially free from contamination with replication competent retrovirus, wherein the recombinant retroviral particles carry a vector construct encoding a gene of interest useful in treating the autoimmune disease; and
- (c) re-introducing into the patient a therapeutically effective amount of the population of transduced T cells or non-dividing cells.

31. A method of modulating the activity of a population of T cells or non-dividing cells in a patient comprising:

- (a) obtaining the population of T cells or non-dividing cells from the patient;
- (b) transducing said population of cells *ex vivo* with a preparation of high titer recombinant retroviral particles substantially free from contamination with replication competent retrovirus, wherein the recombinant retroviral particles carry a vector construct encoding a protein capable of activating a prodrug;
- (c) re-introducing said population of cells into the patient; and
- (c) administering said prodrug to said patient.

32. The method of claim 31 wherein said protein is thymidine kinase.

33. A method according to Claim 1 wherein an envelope protein of the high titer recombinant retroviral particles is an envelope protein derived from a type C retrovirus or from a type D retrovirus.

34. A method according to Claim 1 wherein an envelope protein of the high titer recombinant retroviral particles is an envelope protein is selected from the group consisting of a retroviral amphotropic envelope protein, a retroviral ecotropic envelope

protein, a retroviral polytropic envelope protein, a retroviral xenotropic envelope protein, a gibbon ape leukemia virus envelope protein, and a VSV-g protein.

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Age	50
Sex	Male
Height	175
Weight	65
Education	High school graduate
Marital status	Married
Number of children	2
Occupation	Unemployed
Health insurance	Medicaid
Medication	None
Alcohol consumption	None
Tobacco consumption	None
Exercise	None
Stress	High
Family support	Low
Community resources	Low
Health status	Good
Quality of life	Low
Healthcare access	Low
Healthcare utilization	Low
Healthcare costs	Low
Healthcare satisfaction	Low
Healthcare equity	Low
Healthcare quality	Low
Healthcare safety	Low
Healthcare effectiveness	Low
Healthcare efficiency	Low
Healthcare transparency	Low
Healthcare accountability	Low
Healthcare leadership	Low
Healthcare innovation	Low
Healthcare research	Low
Healthcare education	Low
Healthcare training	Low
Healthcare development	Low
Healthcare improvement	Low
Healthcare reform	Low
Healthcare change	Low
Healthcare progress	Low
Healthcare future	Low
Healthcare vision	Low
Healthcare mission	Low
Healthcare values	Low
Healthcare principles	Low
Healthcare beliefs	Low
Healthcare attitudes	Low
Healthcare behaviors	Low
Healthcare outcomes	Low
Healthcare impact	Low
Healthcare legacy	Low
Healthcare heritage	Low
Healthcare tradition	Low
Healthcare culture	Low
Healthcare identity	Low
Healthcare reputation	Low
Healthcare image	Low
Healthcare brand	Low
Healthcare logo	Low
Healthcare slogan	Low
Healthcare tagline	Low
Healthcare motto	Low
Healthcare mantra	Low
Healthcare aphorism	Low
Healthcare proverb	Low
Healthcare saying	Low
Healthcare phrase	Low
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Healthcare suggestion	Low
Healthcare advice	Low
Healthcare counsel	Low
Healthcare guidance	Low
Healthcare instruction	Low
Healthcare direction	Low
Healthcare leadership	Low
Healthcare management	Low
Healthcare administration	Low
Healthcare organization	Low
Healthcare structure	Low
Healthcare system	Low
Healthcare network	Low
Healthcare community	Low
Healthcare society	Low
Healthcare culture	Low
Healthcare identity	Low
Healthcare reputation	Low
Healthcare image	Low
Healthcare brand	Low
Healthcare logo	Low
Healthcare slogan	Low
Healthcare tagline	Low
Healthcare motto	Low
Healthcare mantra	Low
Healthcare aphorism	Low
Healthcare proverb	Low
Healthcare saying	Low
Healthcare phrase	Low
Healthcare expression	Low
Healthcare statement	Low
Healthcare declaration	Low
Healthcare assertion	Low
Healthcare affirmation	Low
Healthcare confirmation	Low
Healthcare validation	Low
Healthcare verification	Low
Healthcare authentication	Low
Healthcare certification	Low
Healthcare accreditation	Low
Healthcare authorization	Low
Healthcare approval	Low
Healthcare endorsement	Low
Healthcare recommendation	Low
Healthcare suggestion	Low
Healthcare advice	Low
Healthcare counsel	Low
Healthcare guidance	Low
Healthcare instruction	Low
Healthcare direction	Low
Healthcare leadership	Low
Healthcare management	Low
Healthcare administration	Low
Healthcare organization	Low
Healthcare structure	Low
Healthcare system	Low
Healthcare network	Low
Healthcare community	Low
Healthcare society	Low
Healthcare culture	Low
Healthcare identity	Low
Healthcare reputation	Low
Healthcare image	Low
Healthcare brand	Low
Healthcare logo	Low
Healthcare slogan	Low
Healthcare tagline	Low
Healthcare motto	Low
Healthcare mantra	Low
Healthcare aphorism	Low
Healthcare proverb	Low
Healthcare saying	Low
Healthcare phrase	Low
Healthcare expression	Low
Healthcare statement	Low
Healthcare declaration	Low
Healthcare assertion	Low
Healthcare affirmation	Low
Healthcare confirmation	Low
Healthcare validation	Low
Healthcare verification	Low
Healthcare authentication	Low
Healthcare certification	Low
Healthcare accreditation	Low
Healthcare authorization	Low
Healthcare approval	Low
Healthcare endorsement	Low
Healthcare recommendation	Low
Healthcare suggestion	Low
Healthcare advice	Low
Healthcare counsel	Low
Healthcare guidance	Low
Healthcare instruction	Low
Healthcare direction	Low
Healthcare leadership	Low
Healthcare management	Low
Healthcare administration	Low
Healthcare organization	Low
Healthcare structure	Low
Healthcare system	Low
Healthcare network	Low
Healthcare community	Low
Healthcare society	Low
Healthcare culture	Low
Healthcare identity	Low
Healthcare reputation	Low
Healthcare image	Low
Healthcare brand	Low
Healthcare logo	Low
Healthcare slogan	Low
Healthcare tagline	Low
Healthcare motto	Low
Healthcare mantra	Low
Healthcare aphorism	Low
Healthcare proverb	Low
Healthcare saying	Low
Healthcare phrase	Low
Healthcare expression	Low
Healthcare statement	Low
Healthcare declaration	Low
Healthcare assertion	Low
Healthcare affirmation	Low
Healthcare confirmation	Low
Healthcare validation	Low
Healthcare verification	Low
Healthcare authentication	Low
Healthcare certification	Low
Healthcare accreditation	Low
Healthcare authorization	Low
Healthcare approval	Low
Healthcare endorsement	Low
Healthcare recommendation	Low
Healthcare suggestion	Low
Healthcare advice	Low